

# Trex: Can we predict TCR- epitope interaction with deep learning

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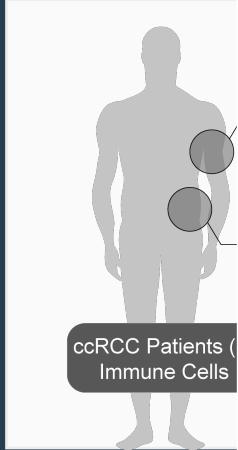
# Conflicts of Interest

- Starting a position as Head of Computational Biology for Omniscope looking at deep TCR/BCR sequencing in diagnosis/prognosis
- Trex is not a product, portion of pipeline, or part of the Omniscope LLC

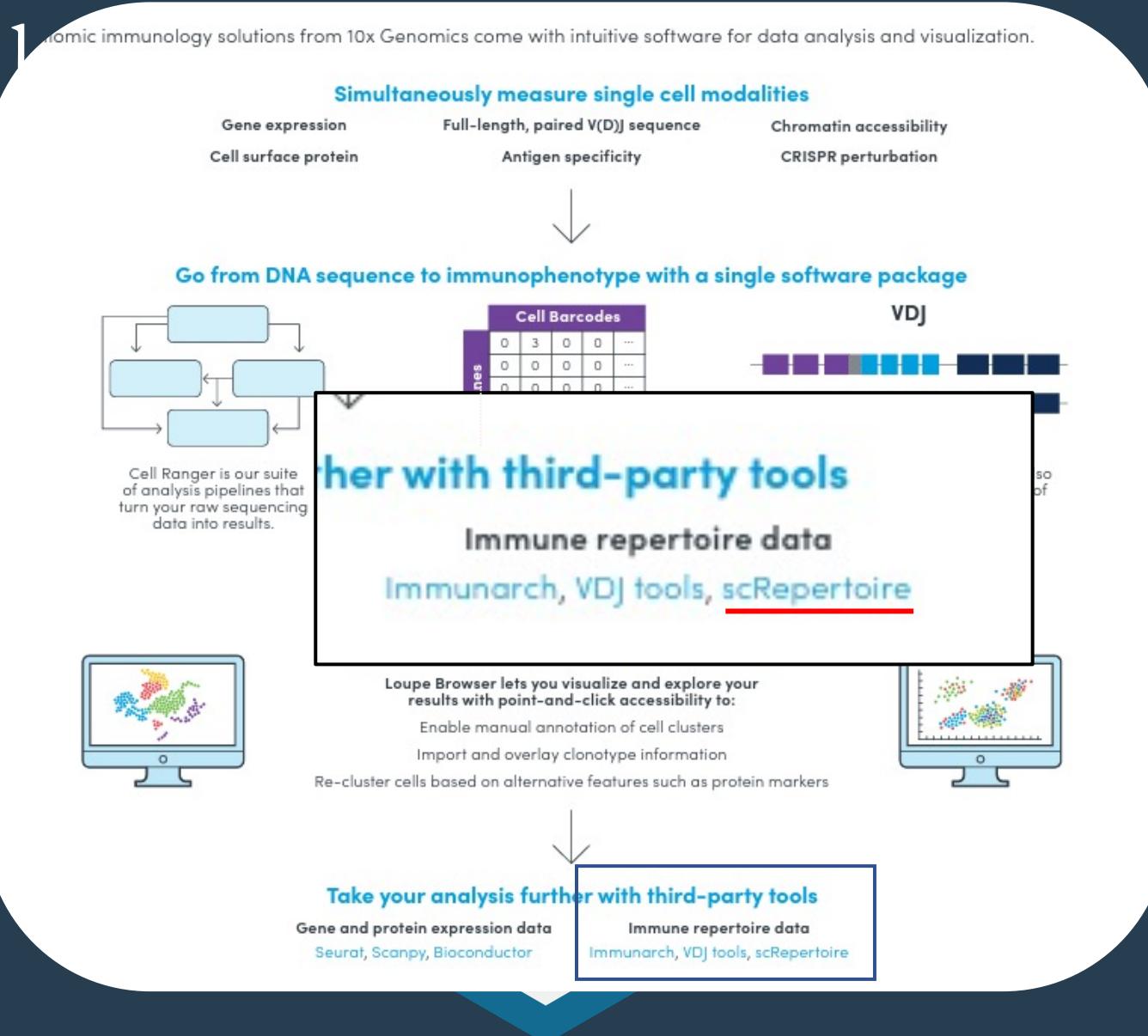
# 10x Genomics Multiomic Single-Cell Immunology

T cells, a k

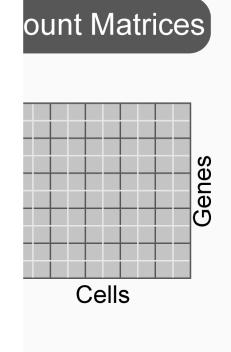
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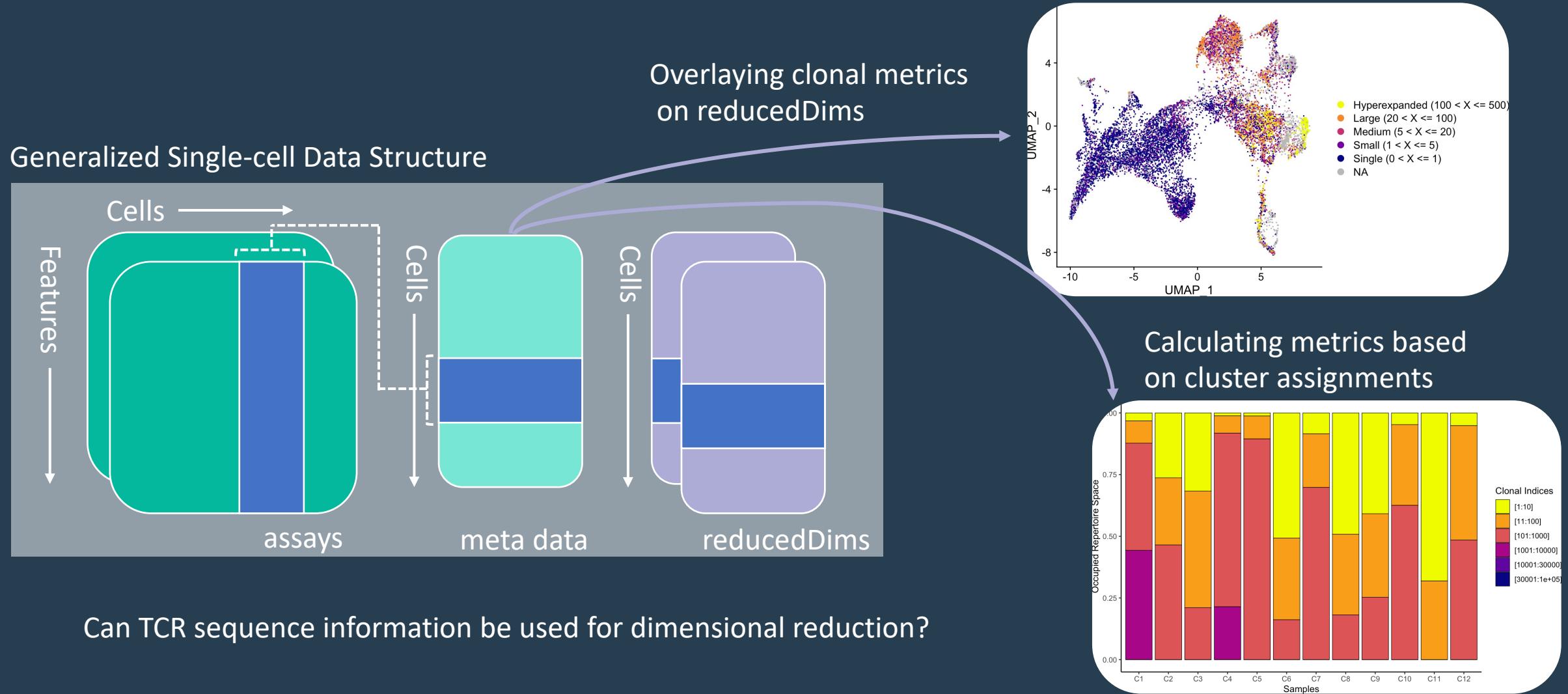
combining TCR/BCR  
single-cell RNA data



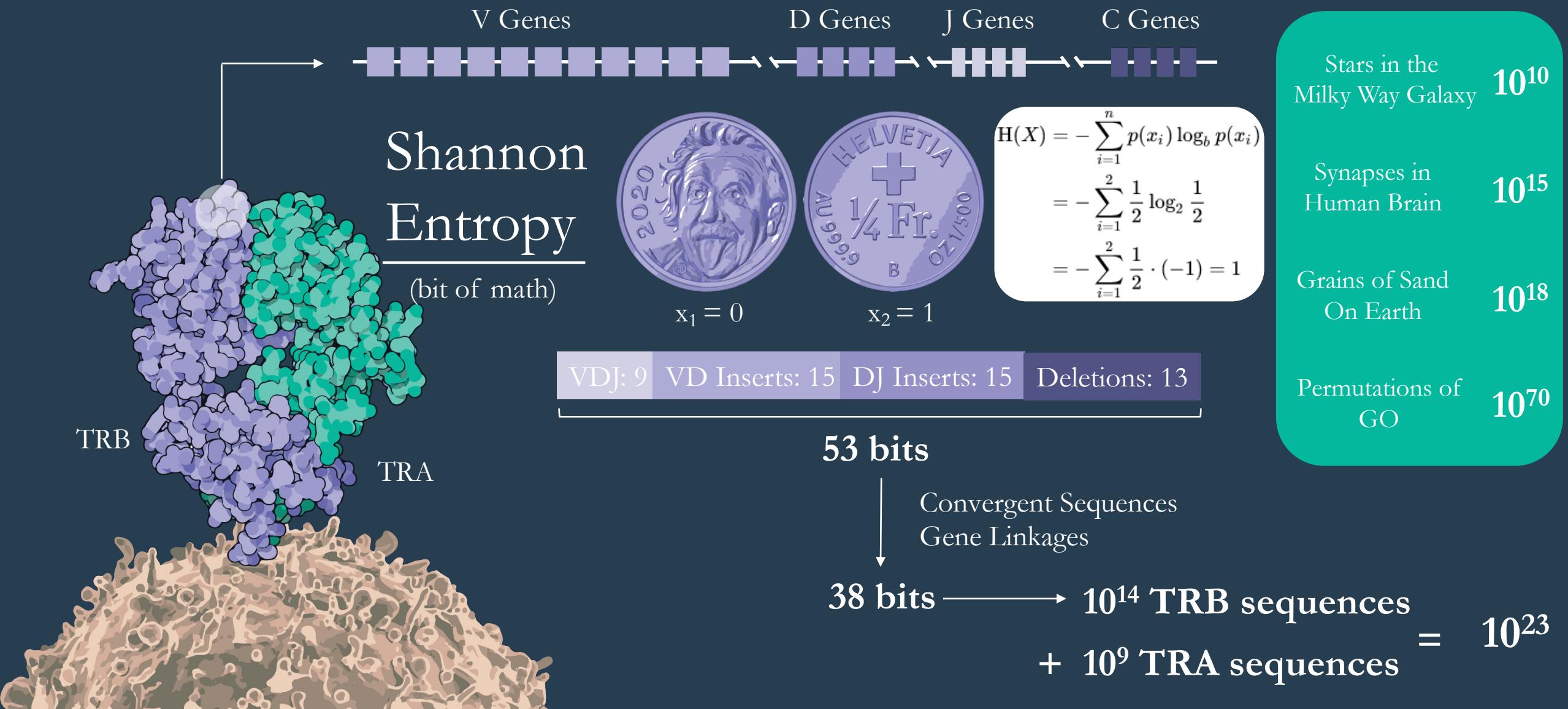
t

- Additional Tool Suggestions
- **Python:** sciripy, dandelion
  - **R:** Platypus

# Limitations of single-cell clonotype approaches

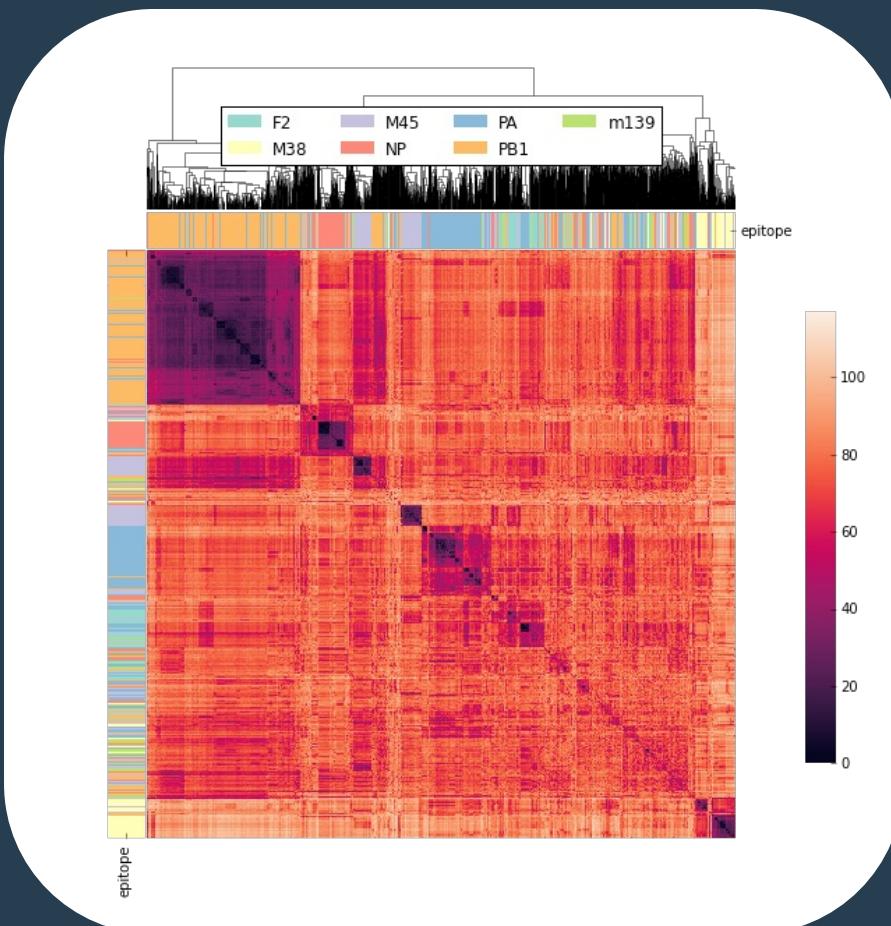


# Leveraging T Cell Receptor (TCR) Diversity

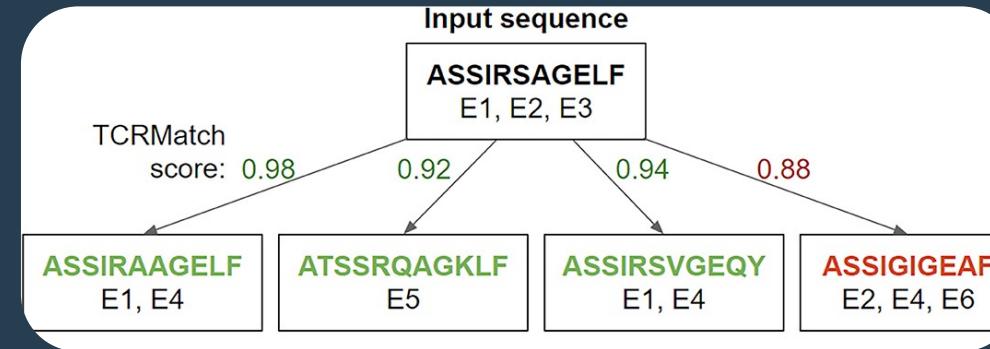


# Current approaches to reduce TCR complexity

TCRdist: Edit Distance of CDR3 sequences



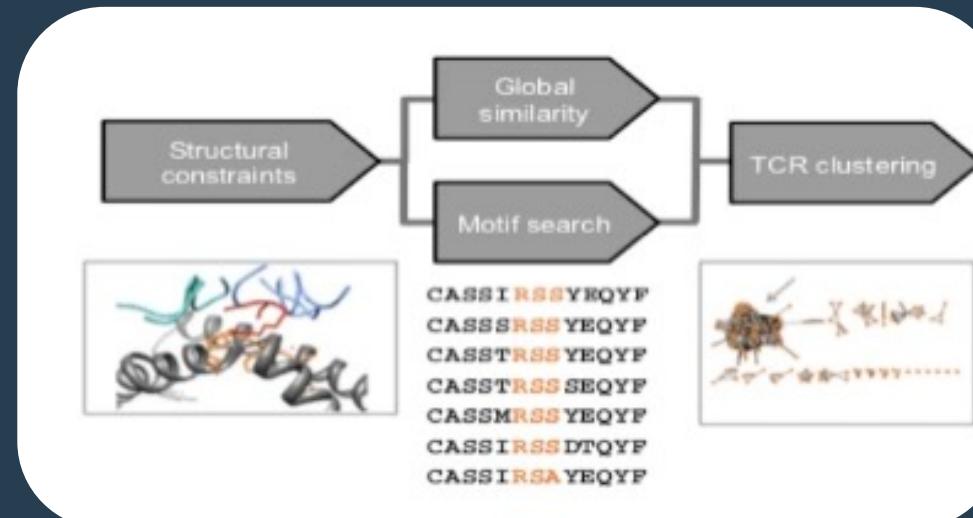
TCRmatch: Edit Distance of CDR3b compared to reference



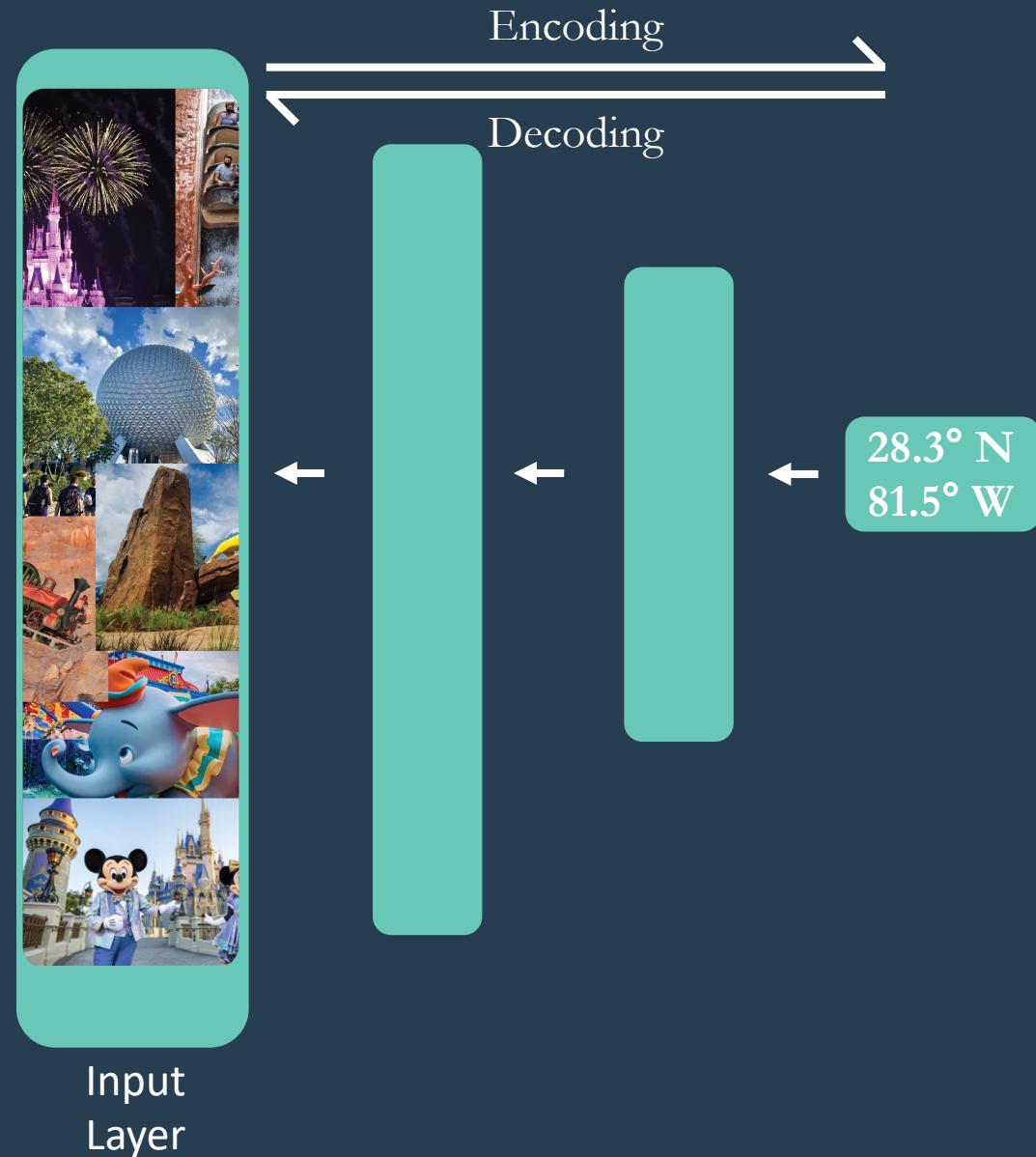
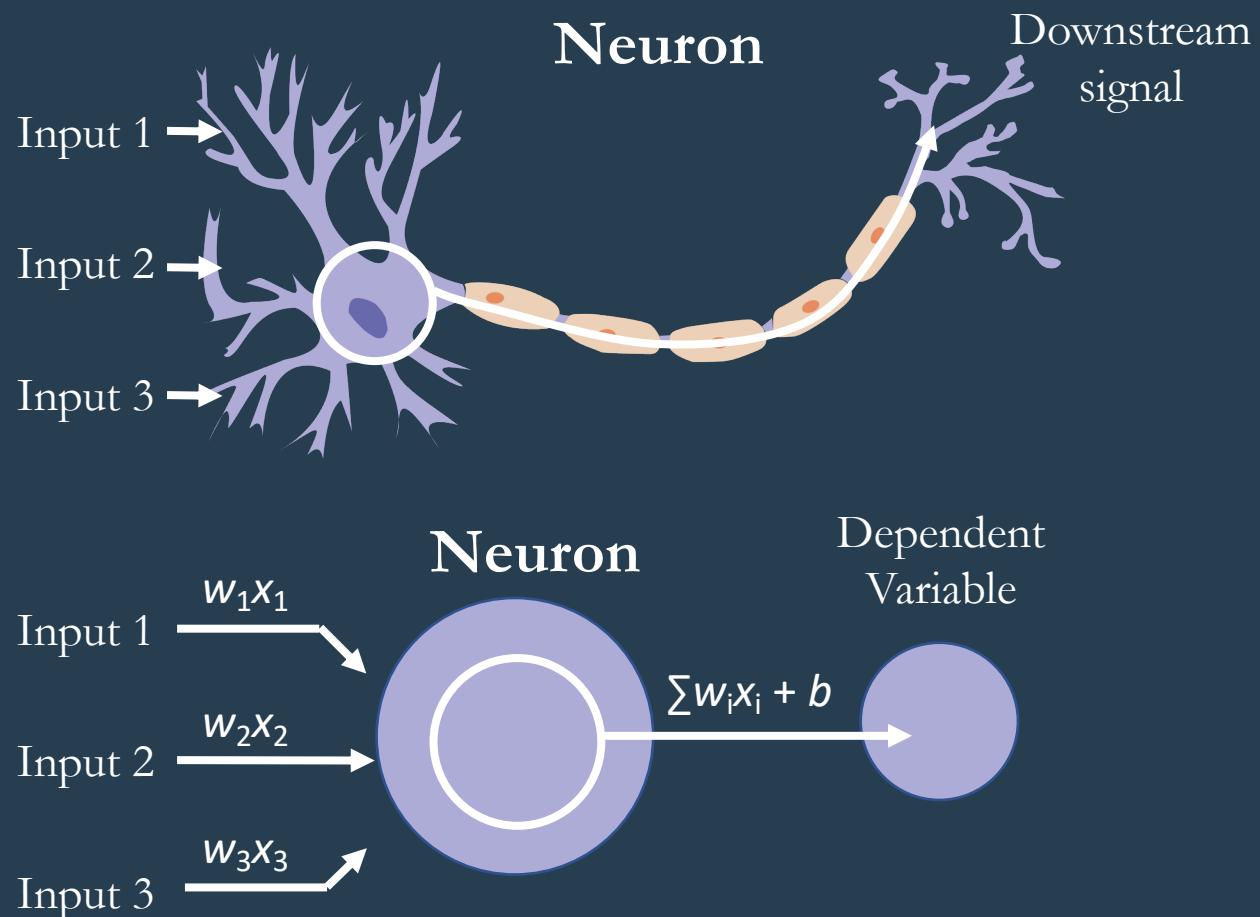
Deep Learning

DeepTCR  
TESSA  
DeepCAT  
pMTnet  
ERGO  
TCellMatch

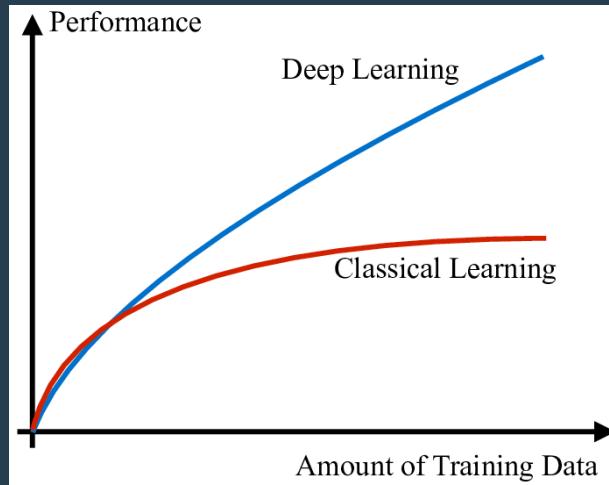
GLIPH: Motif-based TCR evaluation



# What is a neural network?



# Neural network, advantages and limitations



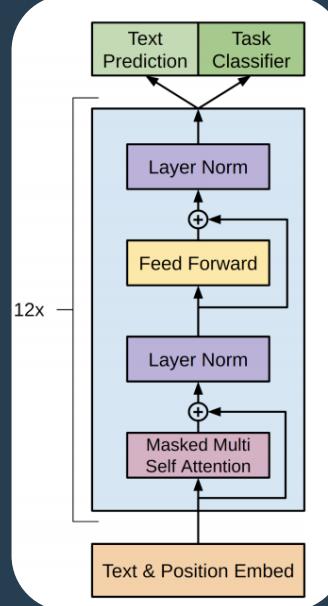
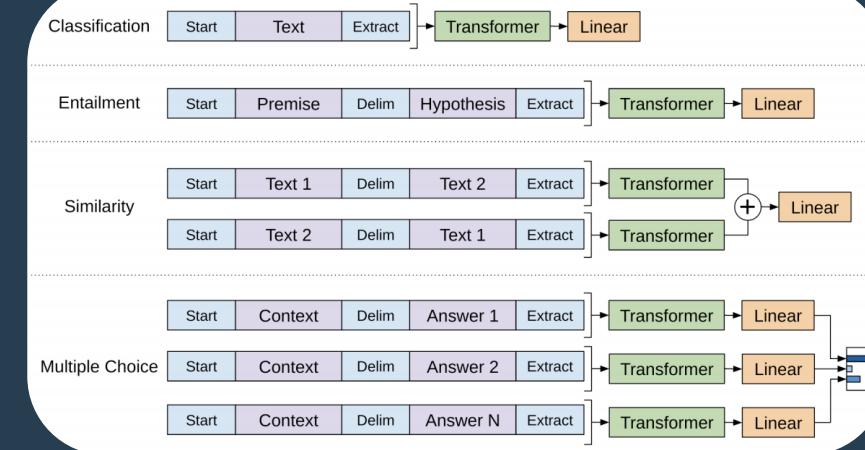
## Deep Learning      Machine Learning

Data Requirement	<b>Large</b>
Accuracy	<b>High</b>
Training Time	<b>Longer</b>
Hardware	<b>GPU</b>

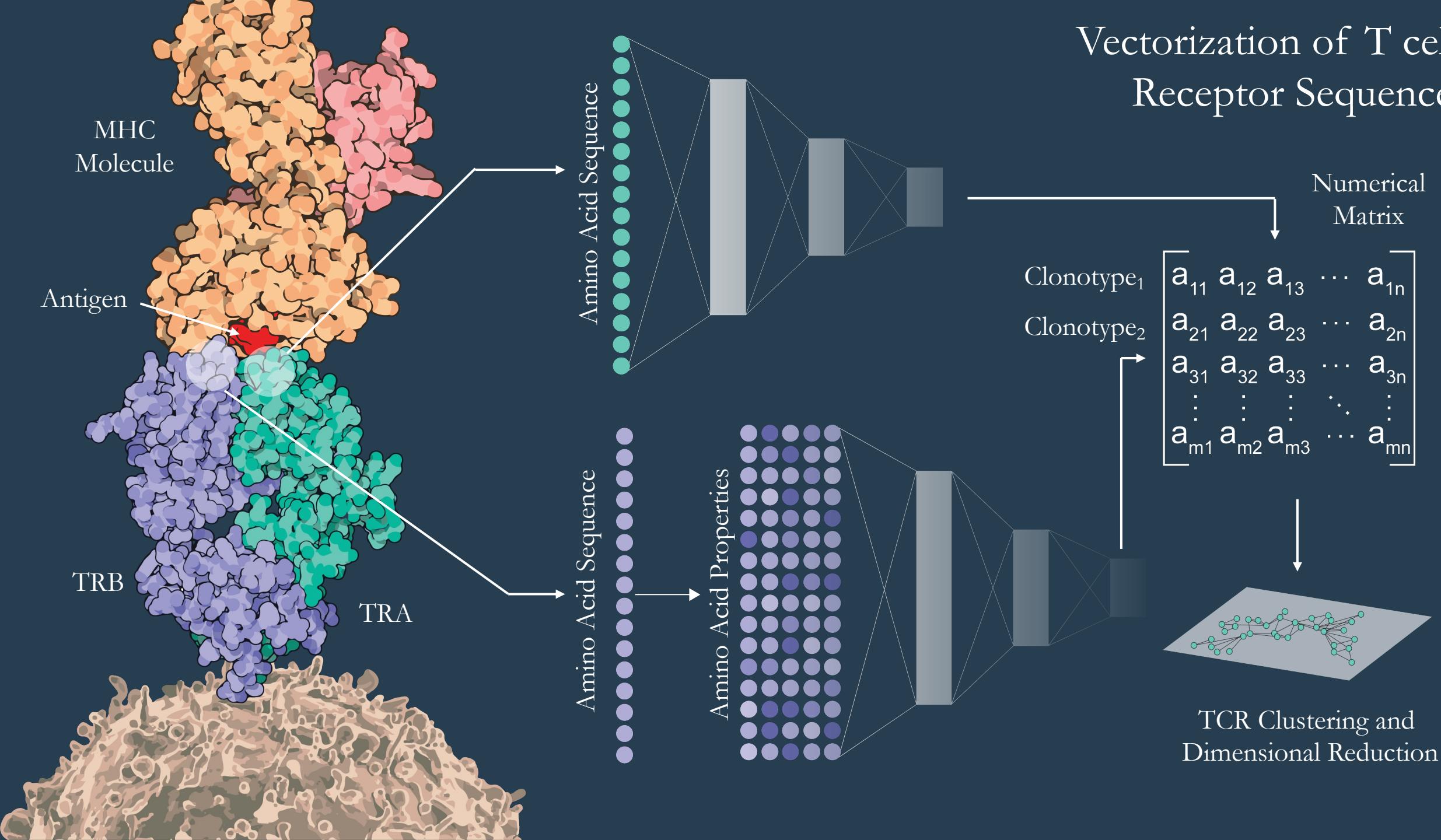
Moderate
Lesser
Shorter
CPU

Emergent Properties

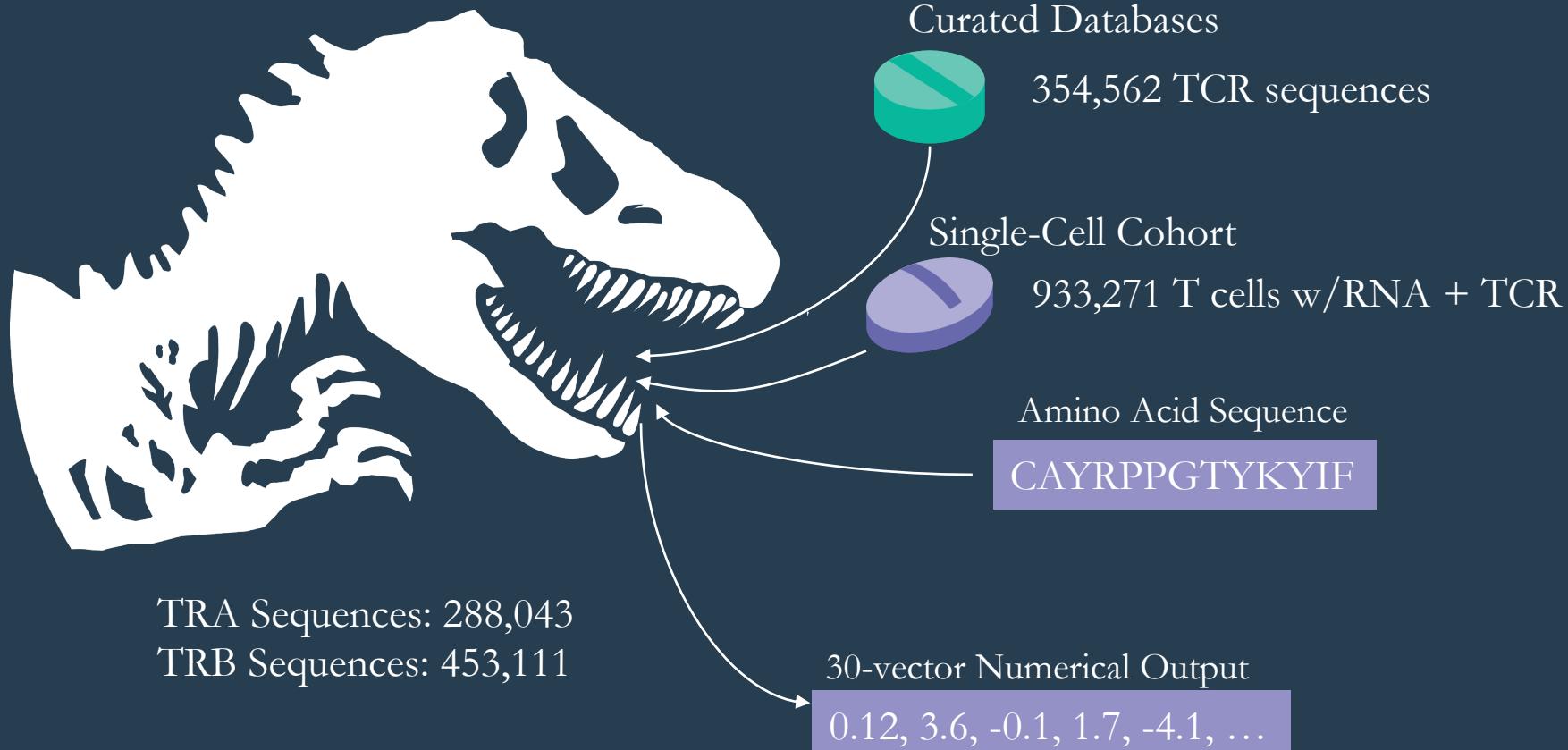
ChatGPT



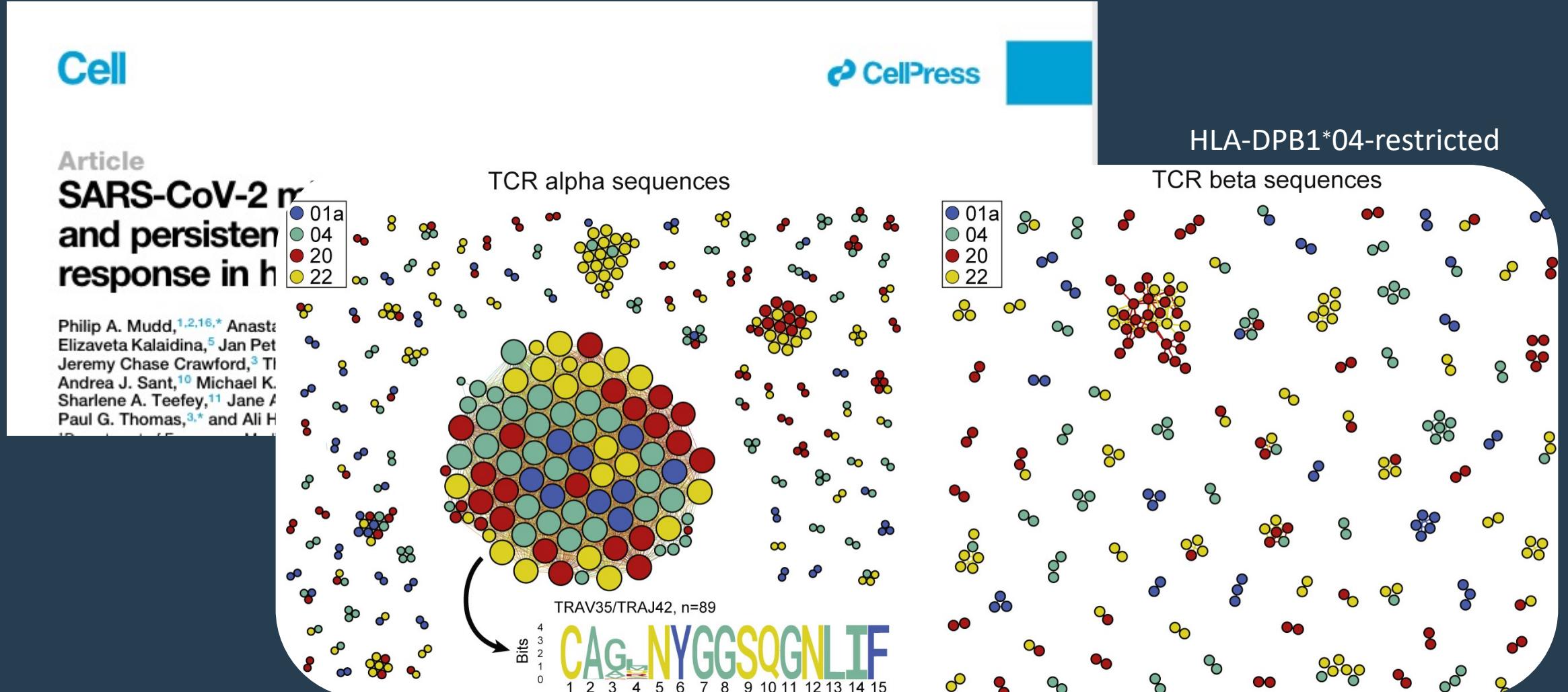
# Vectorization of T cell Receptor Sequences



# Feeding the autoencoder model, Trex

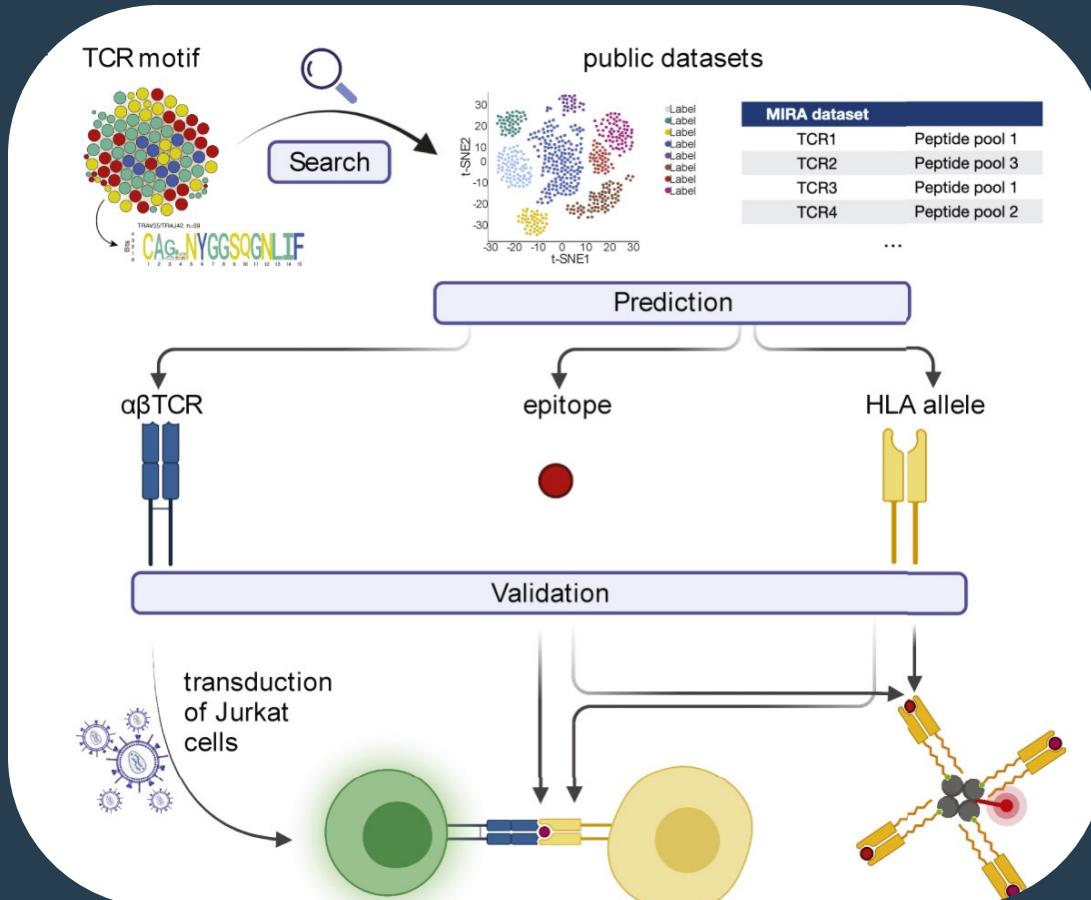


# COVID-19 vaccination – possible application of Trex model

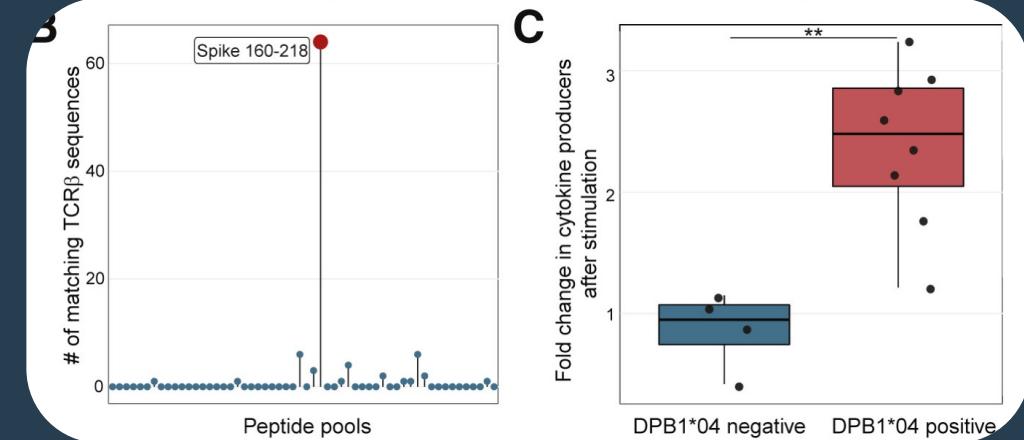


# $S_{167-180}$ epitope discovery and HLA class II tetramer validation

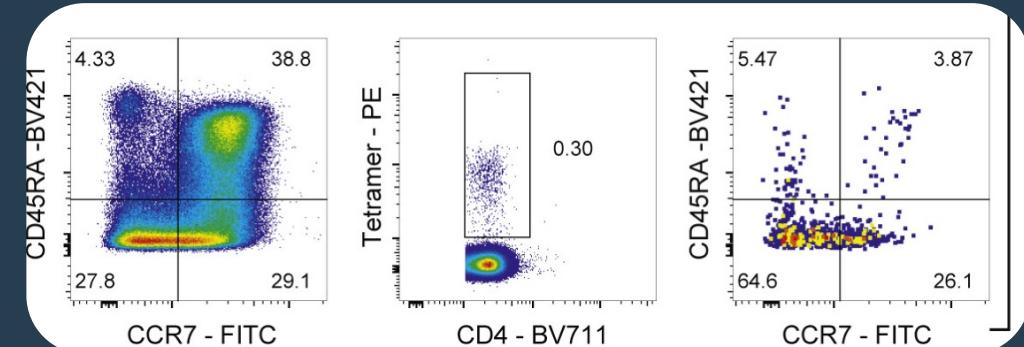
## Response identification process



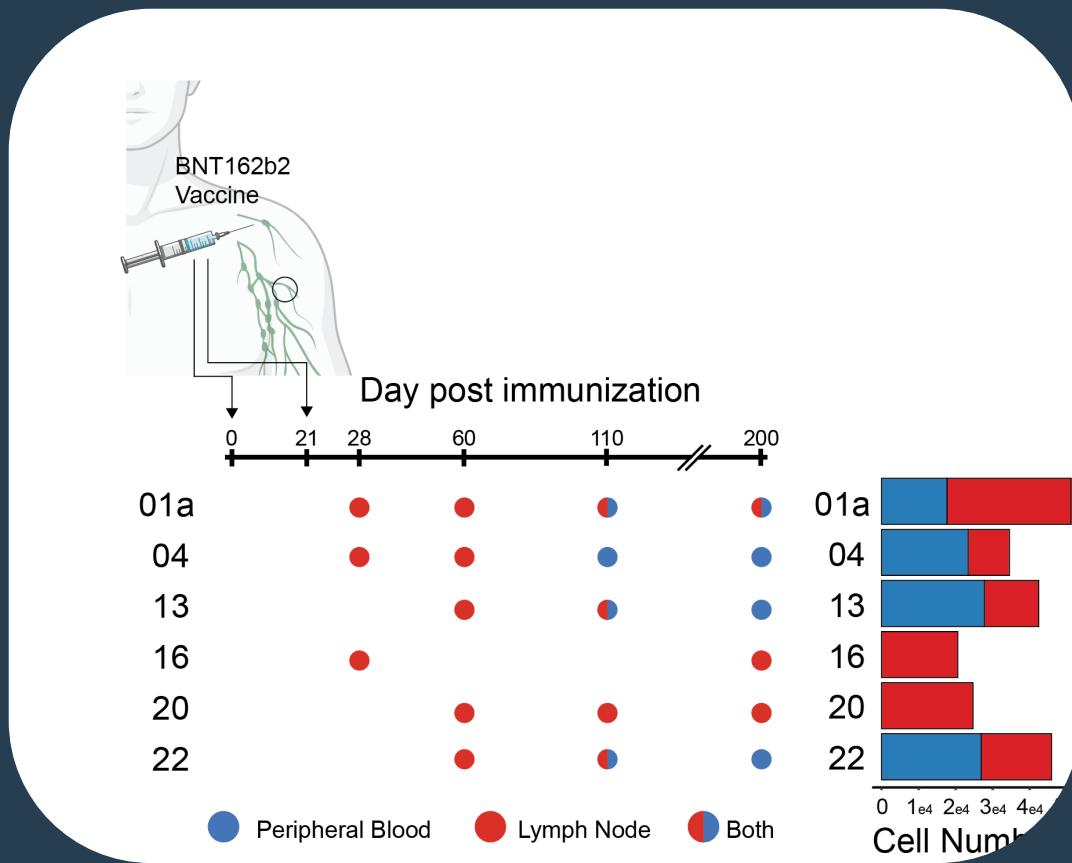
## Identification of epitope region for TCRs



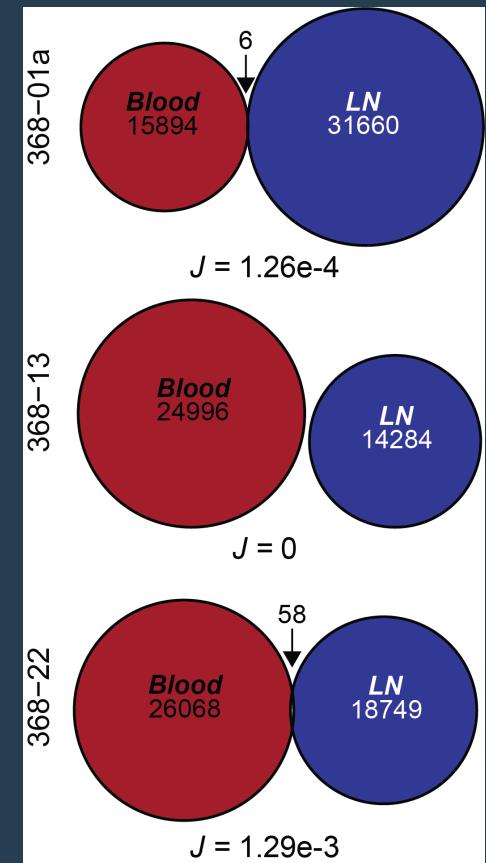
## Validation of tetramer binding



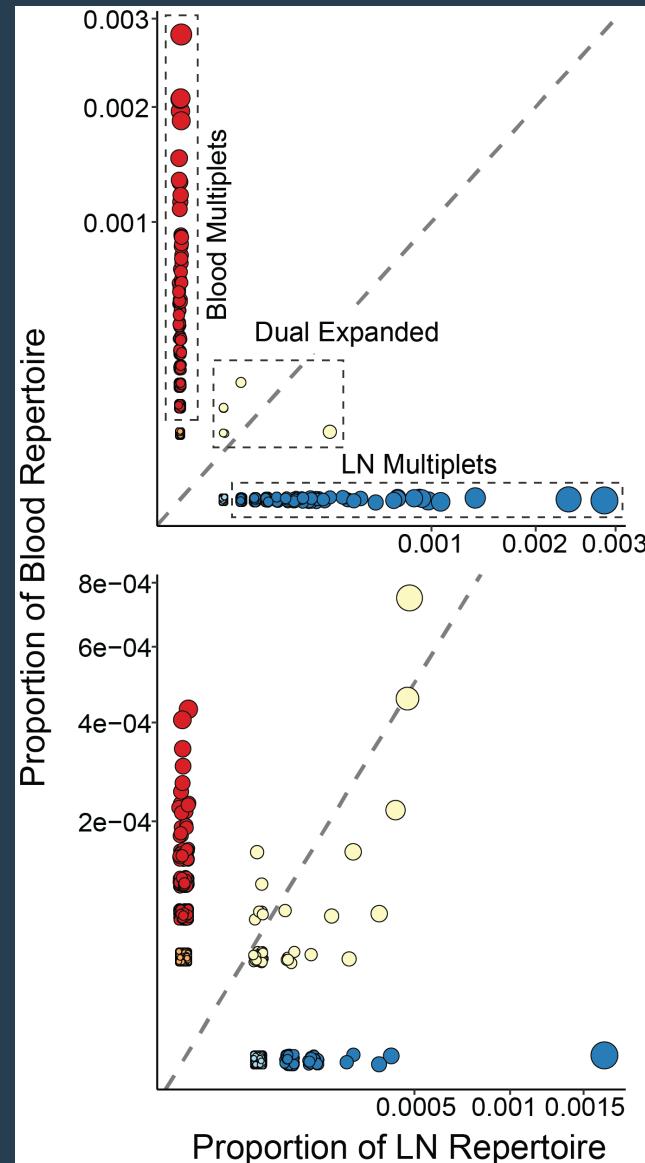
# Data set summary and statistics



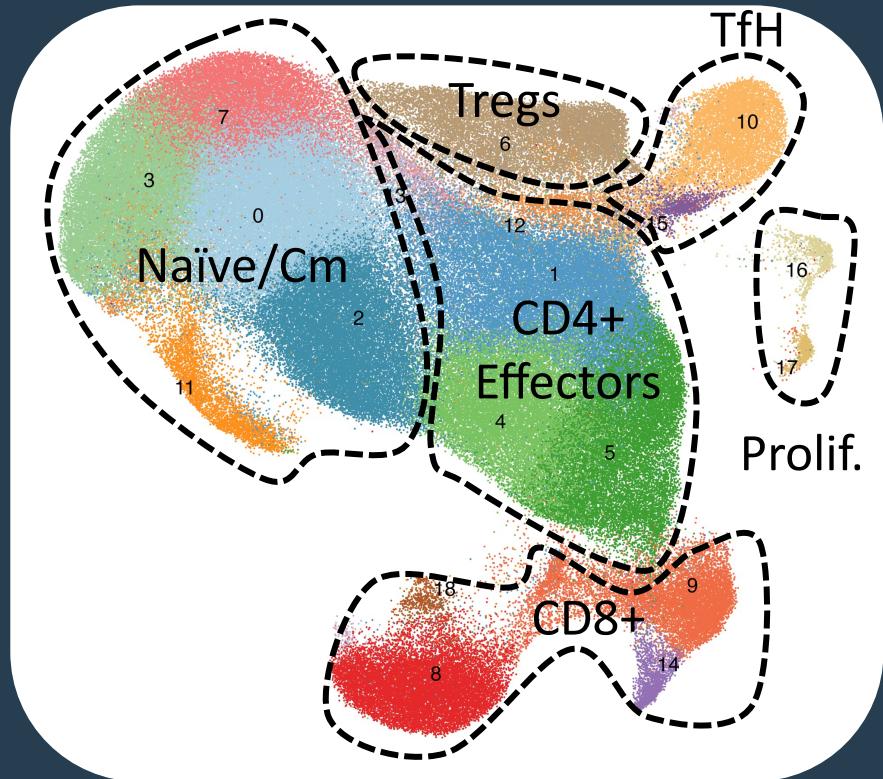
Unique TCR clones



Minimal Overlap between  
LN and Blood

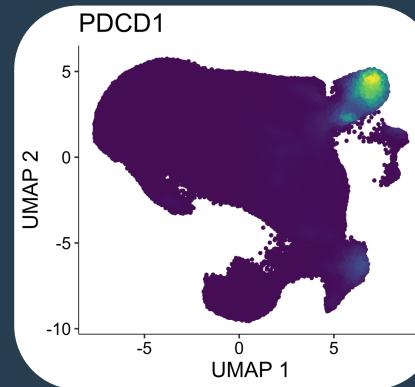
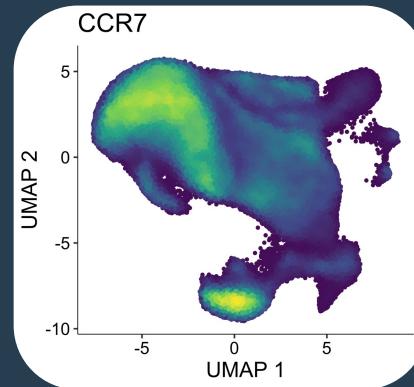
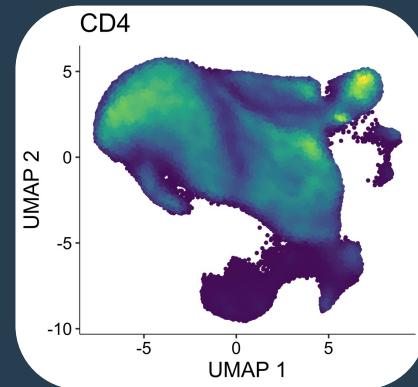
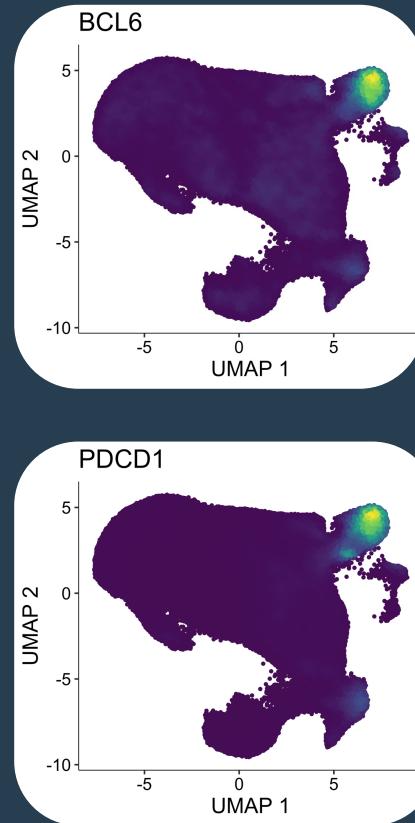
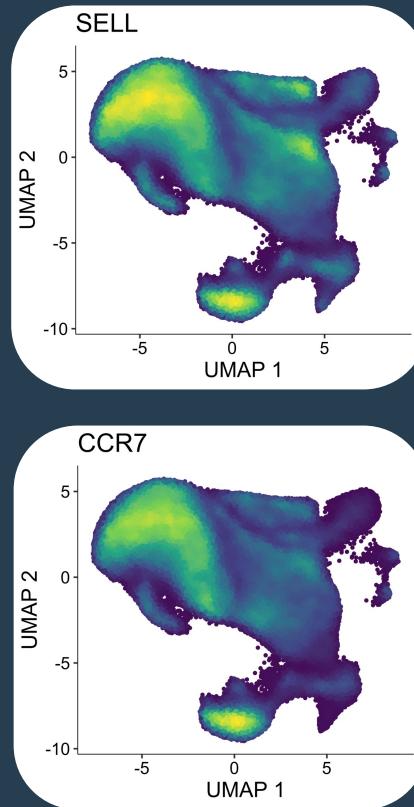
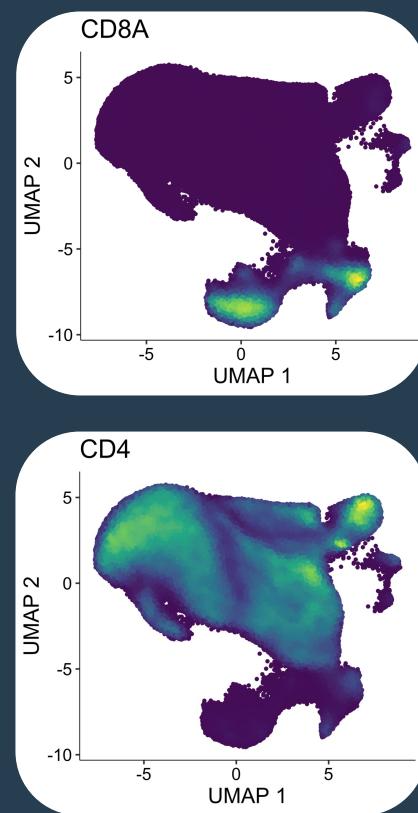


# T-cell Landscape of Lymph Node and Peripheral Blood

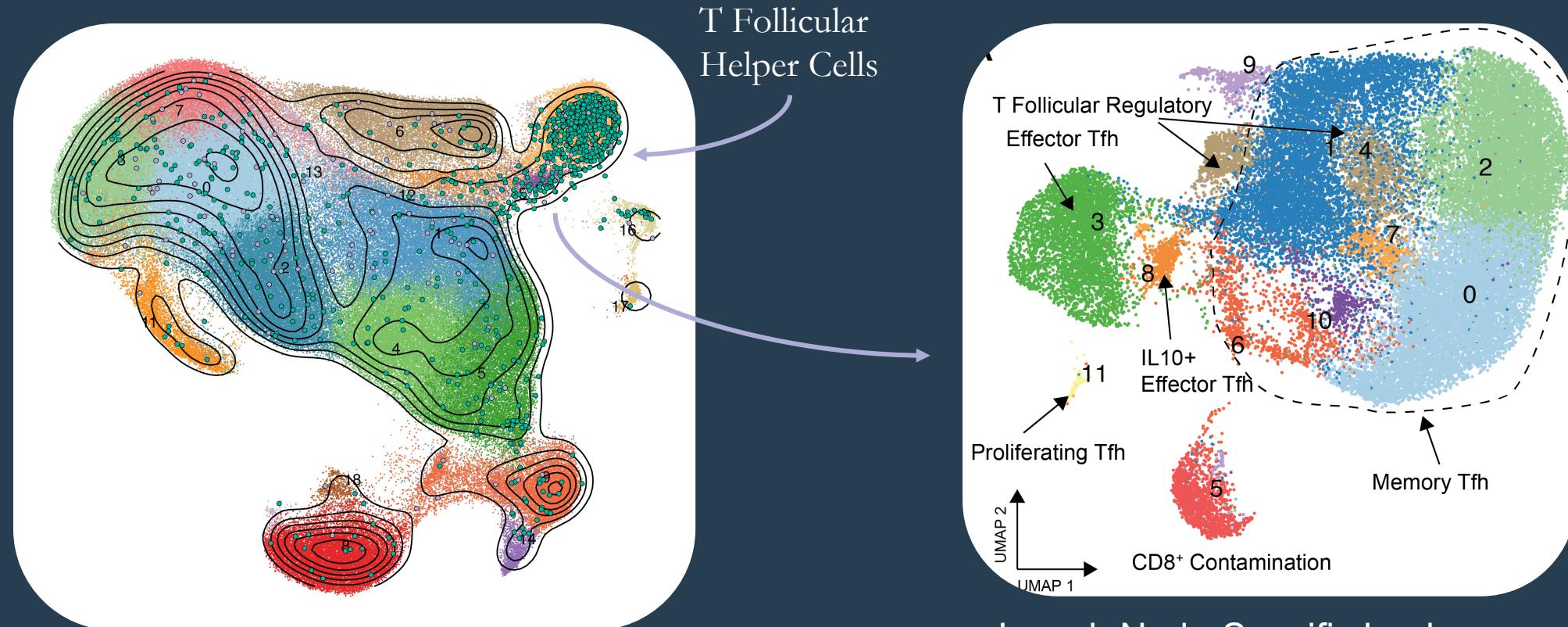


N = 219,284

T cells determined by presence of TCR  
and automated T assignment



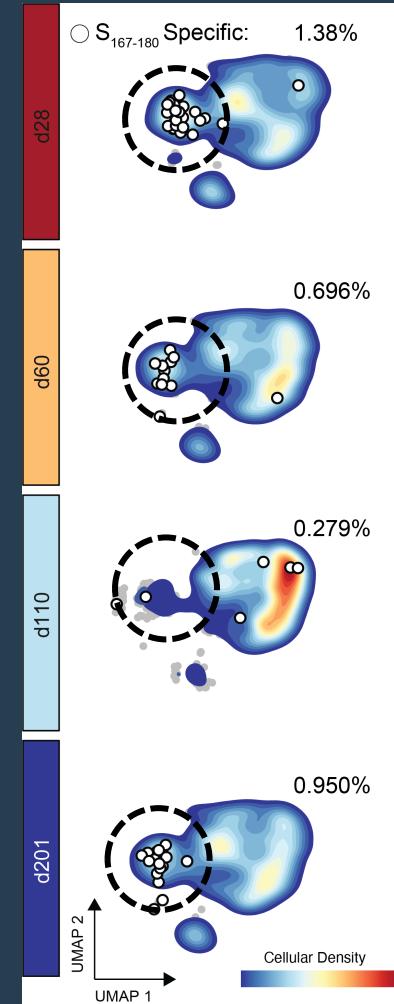
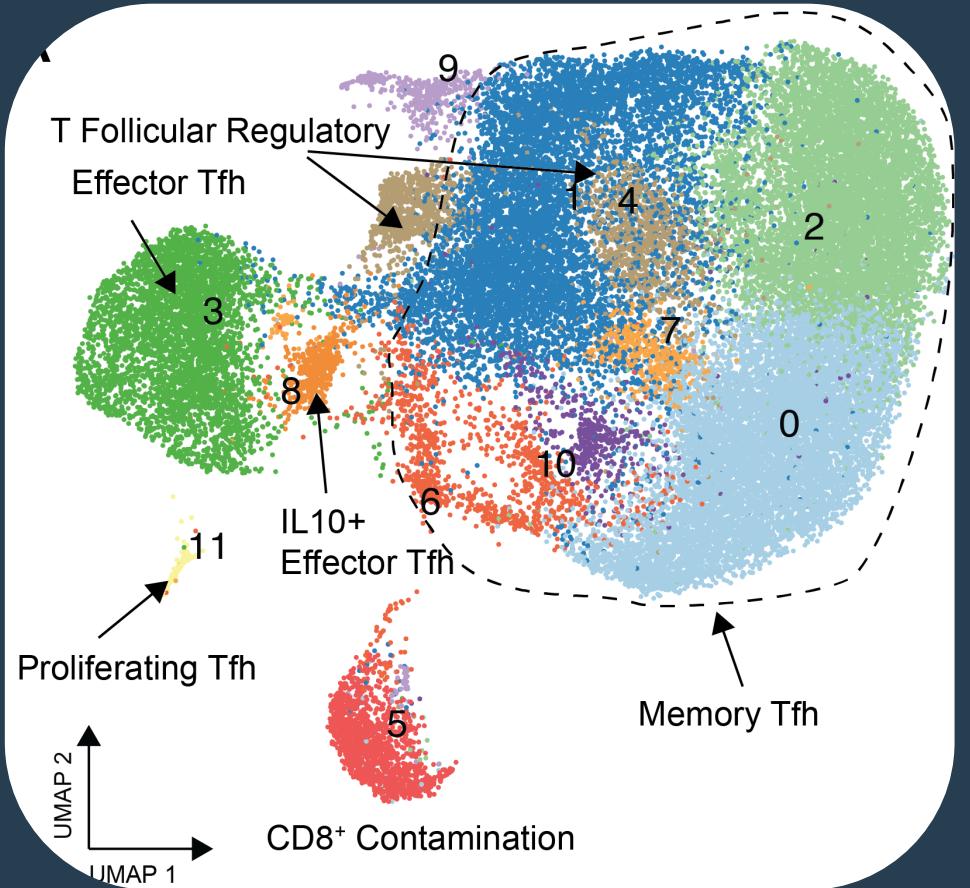
# Spike-specific TCRs localize to T follicular helper cells



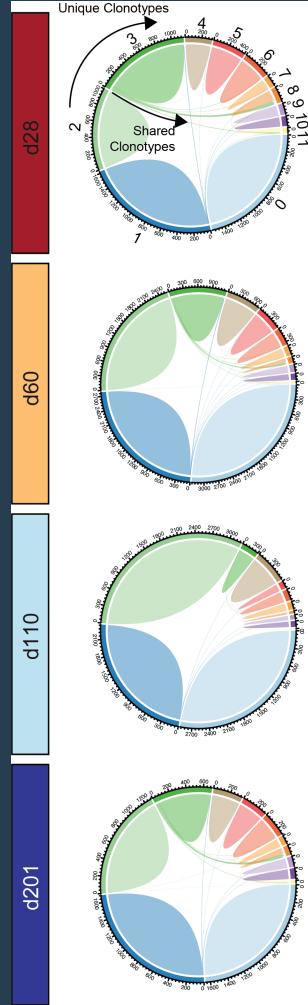
- $\text{Spike}_{167-180}$  TCR
- Other Spike TCR

Previously Validated with Tetramers

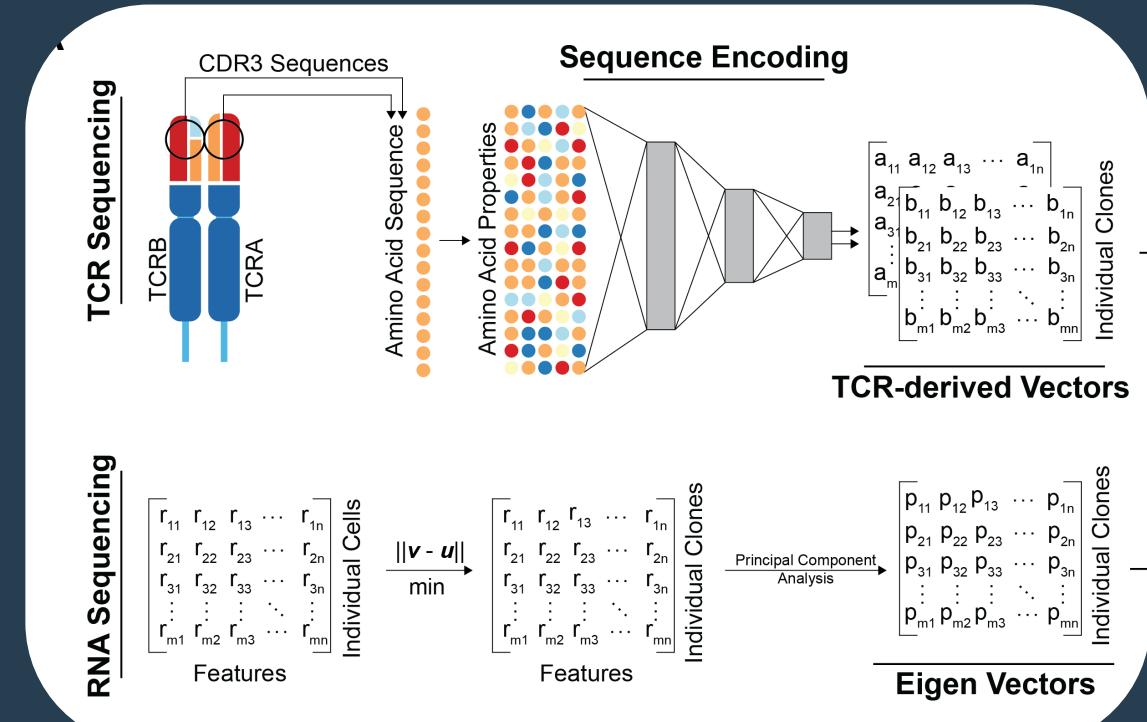
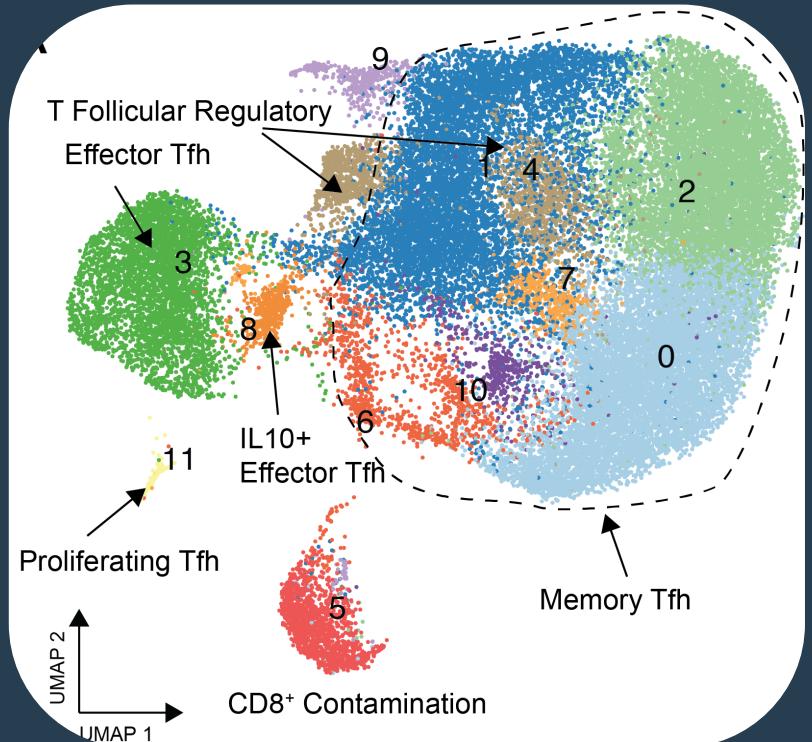
# Spike-specific TCRs are found and shared in Effector Tfh compartment



Shared clones from C3 ↔ C8  
exclusively spike-specific

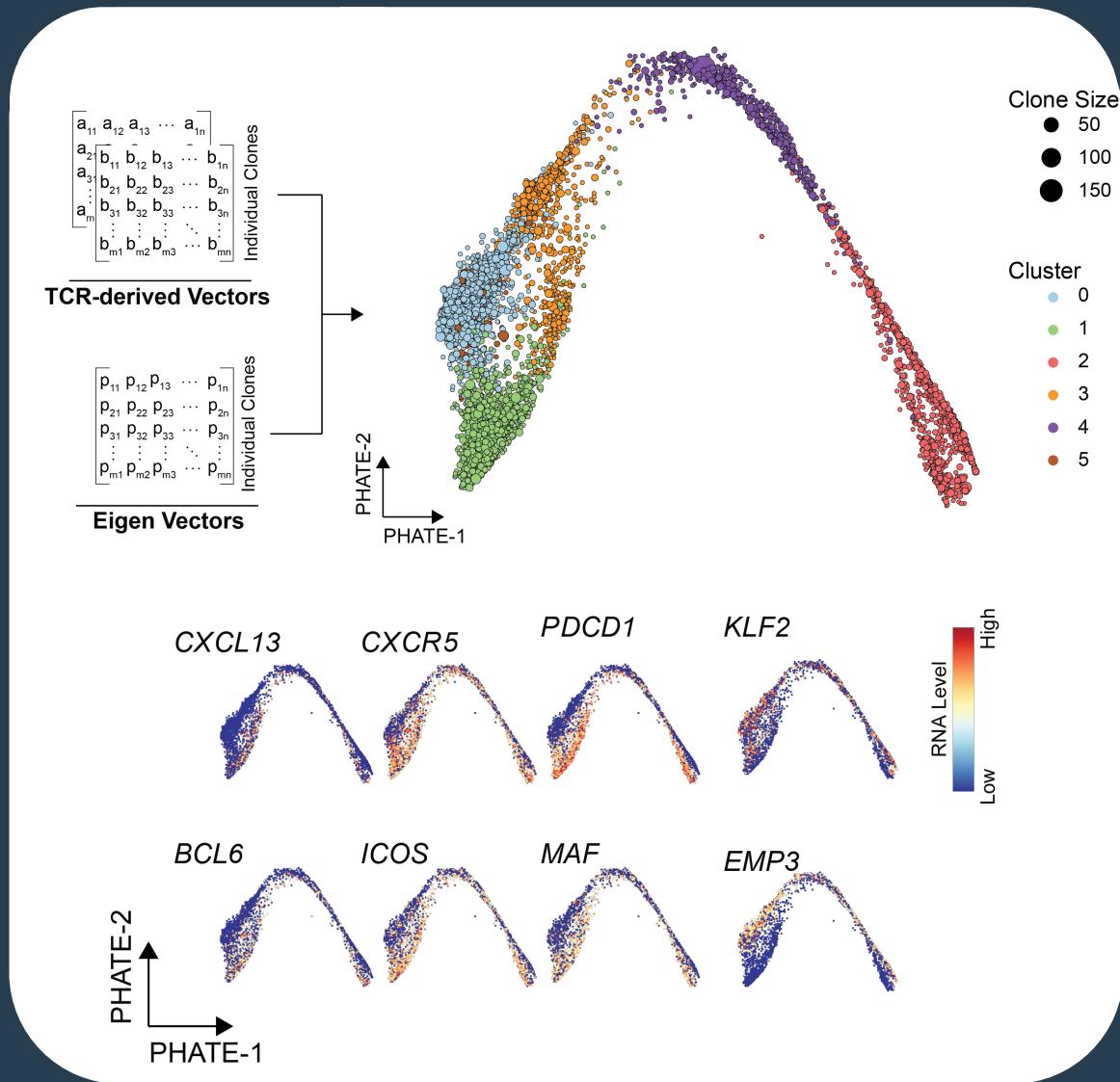


# Can we use the TCR and RNA sequences to examine vaccination response?

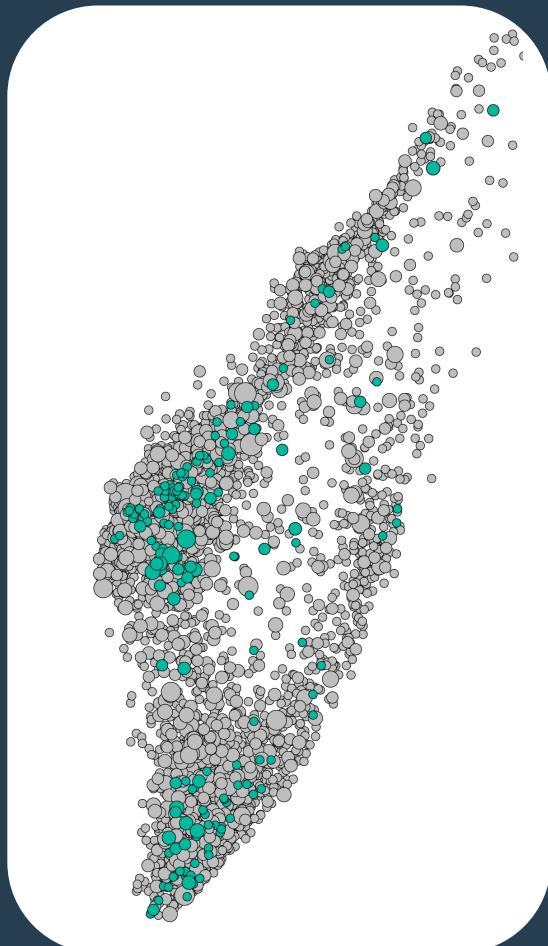


Reducing to single clonotype  
TCR/RNA representation

# TCR/RNA-based lymph node embedding

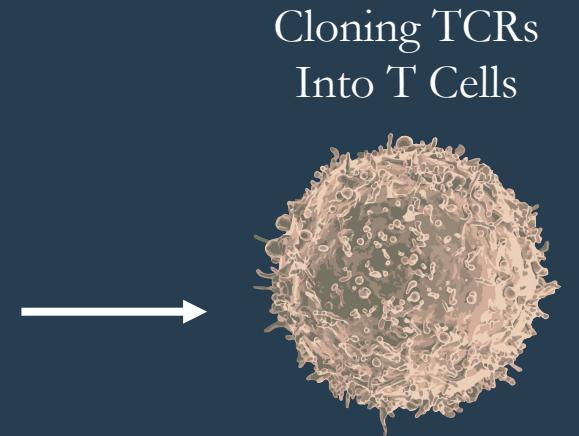
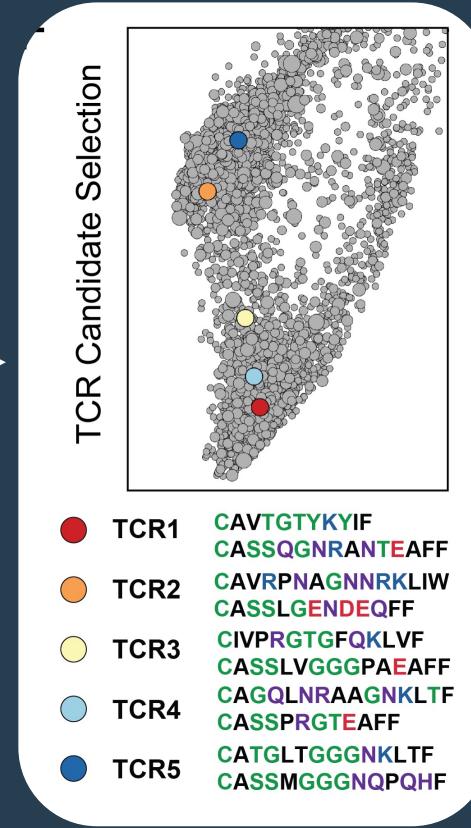
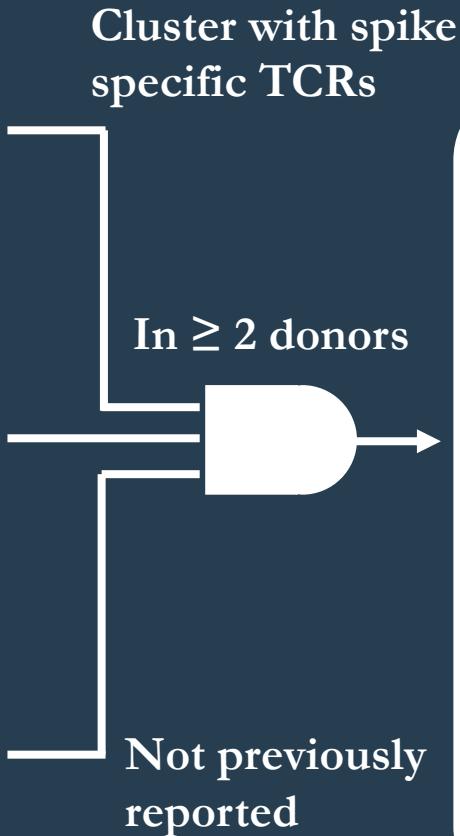
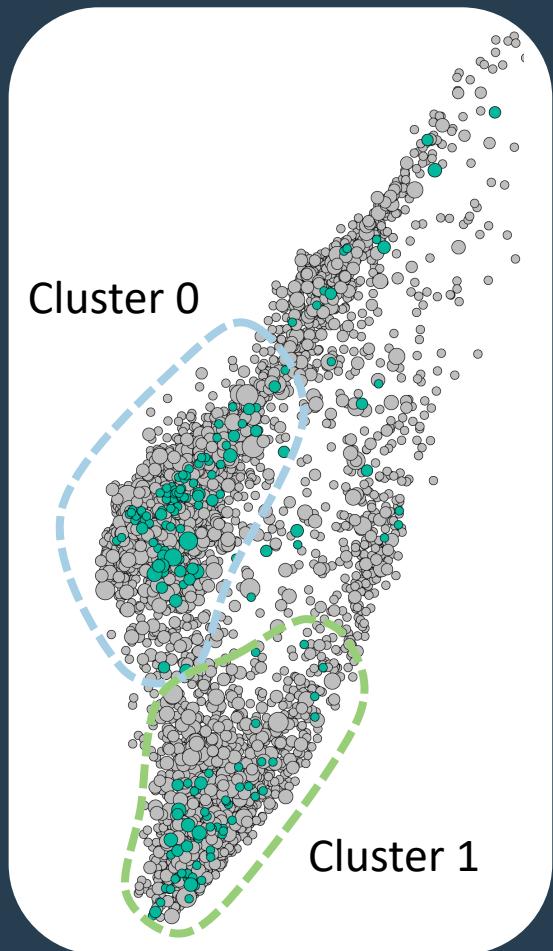


Localization of antigen-specific TCRs



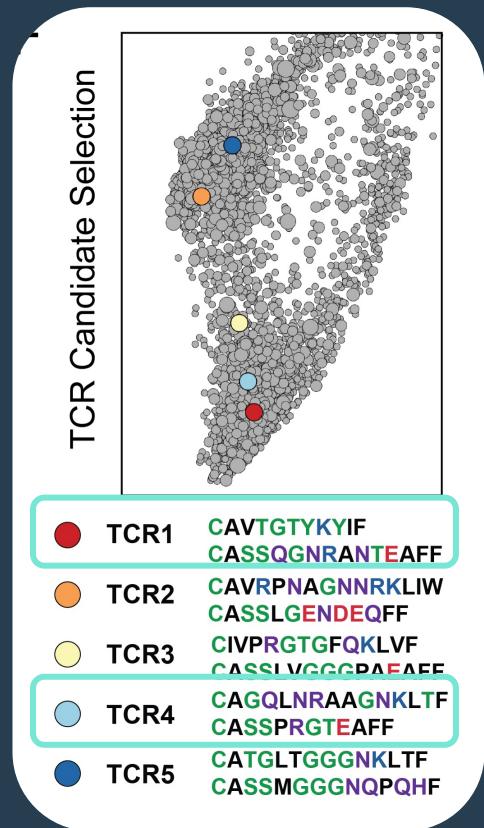
● *Spike<sub>167-180</sub>* TCR

# Selecting the TCRs – Logic gating



First validation of deep-learning-based TCR/Epitope Prediction

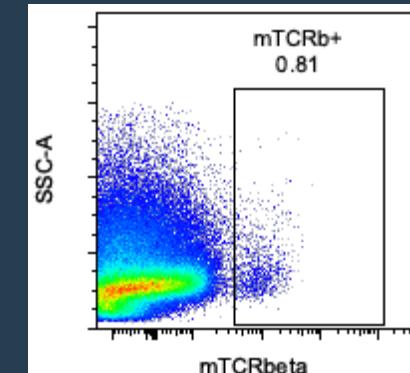
# Preliminary results for candidate spike-specific clones



Clone into chimeric  
TCR construct

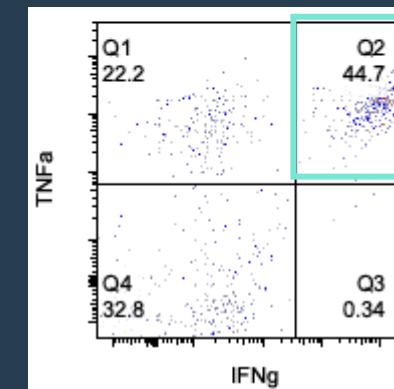
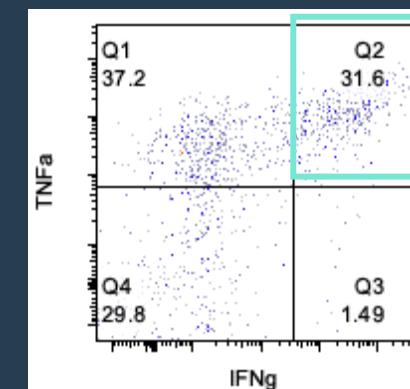
TCR1

S<sub>561-640</sub>



TCR4

S<sub>141-220</sub>

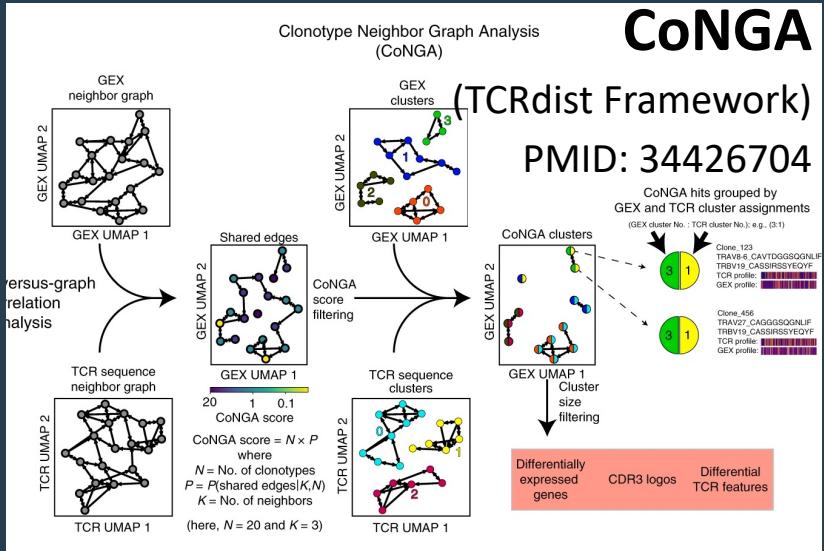


Peptide stimulation

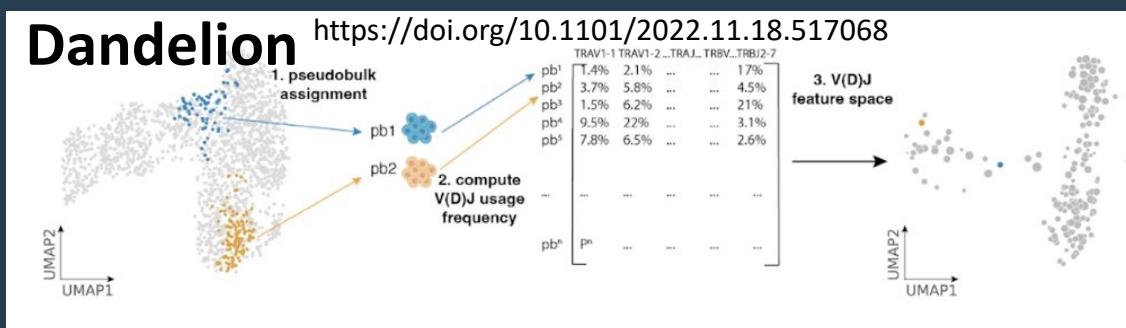
# Remaining points to test

# Benchmarking

# Comparison



Trex



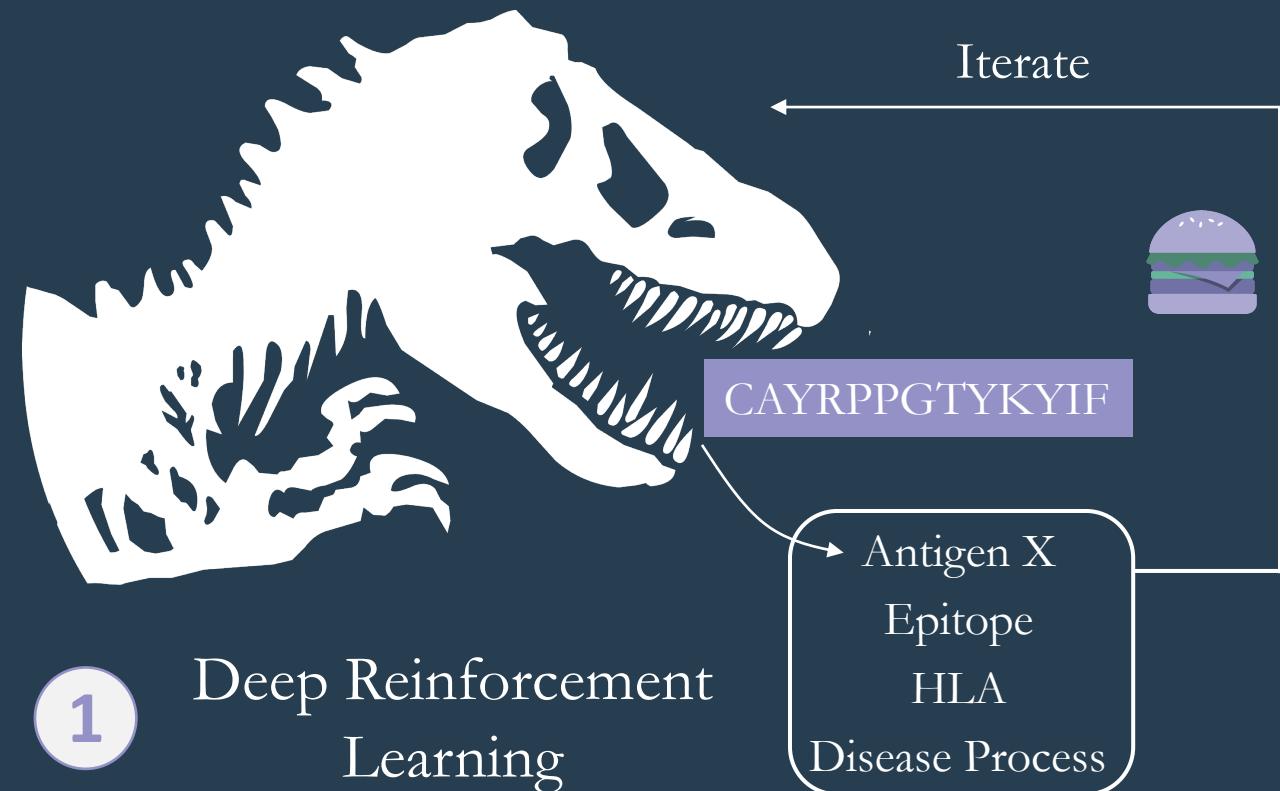
## mRNA Vaccination

## HLA-DPB1\*04-restricted

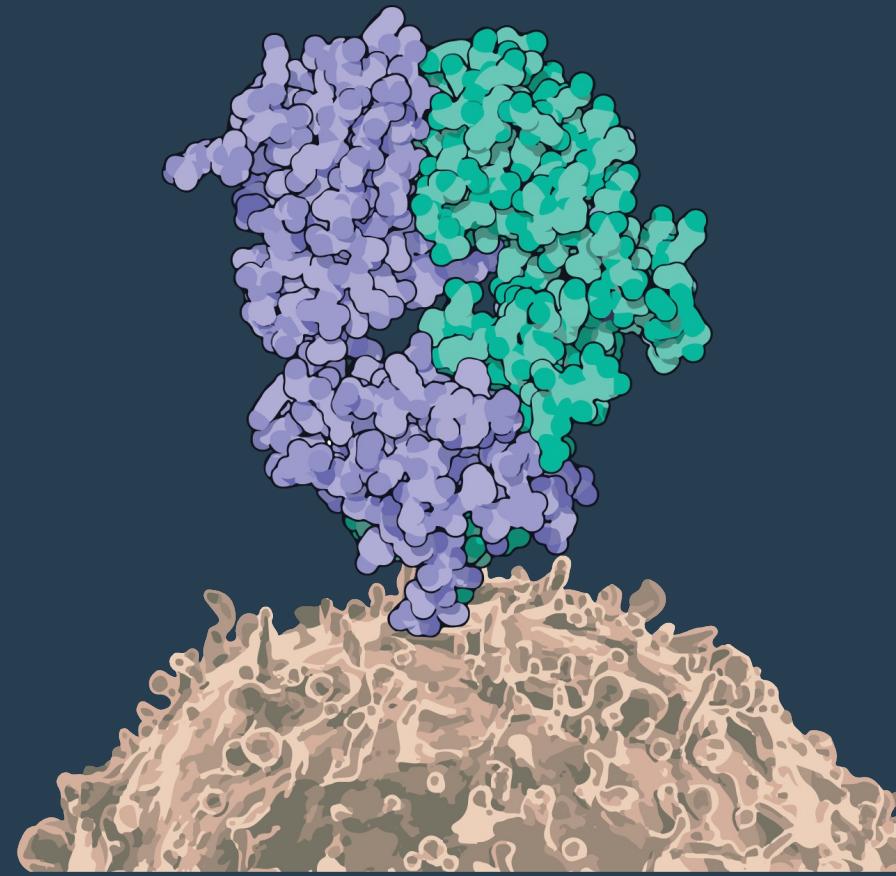
## COVID Infection

- 6 patients
  - Moderate/Severe

# Future Directions



- 2 High Resolution Map of Antigen/TCR
- 3 Train models with Additional Features (Vgenes, HLA, etc)



# Acknowledgements



**Ali Ellebedy**

COVID-19 Cohort  
In vitro validation



**Philip Mudd**



**Michael Quinn**

Sample Isolation  
and Sequencing

Funding for the research came from the Department of Emergency Medicine, Washington University, ST Louis.



**Jon Brestoff**

Putting up with me talking  
about autoencoders

# Questions?

